



PATENT  
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Applicant: Johan Adriaan Martens et al. Confirmation No.: 3753  
Serial No.: 10/562,307 Art Unit: 1618  
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Customer No.: 21559  
Title: CRYSTALLINE MESOPOROUS OXIDE BASED MATERIALS USEFUL  
FOR THE FIXATION AND CONTROLLED RELEASE OF DRUGS

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DECLARATION BY DR. ALEXANDER AERTS

I declare:

1. I am an inventor on the subject matter described and claimed in the above-captioned application.
2. I am a postdoctoral researcher at the Katholieke Universiteit Leuven (K.U.L.). K.U.Leuven Research & Development (the technology transfer office of K.U.L.) is the assignee of the above-captioned application.
3. I carried out the experiments described below in Experiments A through C.

EXPERIMENT A

A sol of Silicalite-1 nanoslabs was prepared as described in EXAMPLE 1 of the application by adding 37.32 g tetraethyl orthosilicate (TEOS) (Acros, 98%) to 32.13 g aqueous tetrapropyl-ammonium hydroxide (TPAOH) solution (Alfa, 40 wt%) under stirring. The mixture upon stirring turned into an emulsion and, as the TEOS was hydrolyzed, gradually transformed into a clear sol. To this 30.55 g of water was added and stirring continued for another 24 hours.

Next, Zeotile-4 was prepared as described in EXAMPLE 2 of the application. 10 g of Pluronic® 123 triblock copolymer from BASF ( $\text{EO}_{20}\text{PO}_{70}\text{EO}_{20}$ ) was dissolved in 90 g water under stirring. An amount of 24 g of this copolymer solution was combined with 8 g of 5 M HCl solution. 18 g of nanoslab sol was combined with another 9 g 5M HCl under vigorous stirring. Subsequently, the acidified nanoslab was combined with the acidic triblock copolymer solution. Then the mixture was heated at 90°C under quiescent conditions for 96 h. A solid product was formed and separated from the liquid by centrifugation at 12,000 rpm. The product was washed with water until the pH exceeded a value of 3. The sample was dried at 60°C for 24 h and finally calcined at 350°C for 24 h with a heating rate of 0.5°C min<sup>-1</sup> in air atmosphere. XRD (x-ray diffraction) confirmed the successful synthesis of Zeotile-4.

## EXPERIMENT B

Comparative Experiment according to Kirschhock et al., *Angew. Chem. Int. Ed.* 40(14): 2637-2640 (2001).

A sol of Silicalite-1 nanoslabs was prepared by adding an amount of 2.92 g tetraethyl orthosilicate (TEOS, Acros, 98%) to 2.57 g of a 40 wt.% aqueous solution of tetrapropylammonium hydroxide (TPAOH, 40 wt.% in water, Alfa) under vigorous magnetic stirring in a polypropylene bottle at room temperature. The mixture, upon stirring, turned into an emulsion and, as the TEOS was hydrolyzed, gradually transformed into a clear sol. To this 94.51 g of water was added and stirring continued for another 24 hours.

The clear nanoslab sol was then heated at 90°C for 48 h in a closed polypropylene bottle, under static conditions. After 48 h, the bottle was removed from the oven and quickly cooled to room temperature under flowing water. After the hydrothermal treatment, the sol turned milky, indicating the formation of a suspension of colloidal Silicalite-1 zeolite crystals.

The suspension of Silicalite-1 zeolite crystals was centrifuged at 10,000 rpm for 30 mins resulting in the sedimentation of the Silicalite-1 crystals. The supernatant was decanted, 100 mL of deionized water was added, the crystals were resuspended and again centrifuged. This procedure was repeated until the pH of the supernatant was below 10.

The pellet of sedimented crystals was subsequently dried at 60°C in air. The dried powder was calcined in a porcelain crucible in a muffle furnace at 550°C for 5 h in air. The heating rate was 1°C/min. XRD confirmed the successful synthesis of Silicalite-1 zeolite crystals.

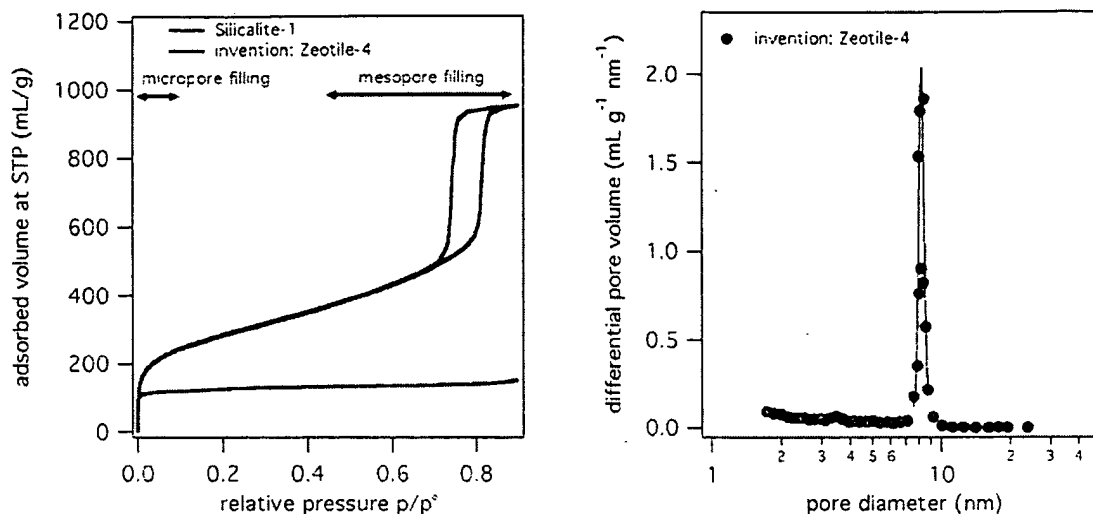
### EXPERIMENT C

Characterization of the porosity of the Zeotile-4 of EXPERIMENT A and the Silicalite-1 zeolite crystals of EXPERIMENT B using nitrogen sorption measurements.

The nitrogen sorption measurements were performed with a Micromeritics Tristar apparatus, at 77K. The sample was pretreated for 9 h at 300°C under a flow of dry air. The results for the Zeotile-4 of EXPERIMENT A and the Silicalite-1 zeolite crystals of EXPERIMENT B are shown in Figure 1 (below). The left graph in Figure 1 shows the nitrogen adsorption and desorption isotherms of Silicalite-1 crystals and Zeotile-4.

The Silicalite-1 crystals only exhibited microporosity as indicated by the upturn in the relative pressure range corresponding to micropore filling but no upturn in the relative pressure range corresponding to mesopore filling. Silicalite-1 crystals thus exhibit a single level of porosity i.e., microporosity.

On the other hand, Zeotile-4 exhibited microporosity as indicated by the upturn in the relative pressure range corresponding to micropore filling and mesoporosity as indicated by the upturn in the relative pressure range corresponding to mesopore filling as indicated by a sharp upturn around  $p/p^\circ = 0.75$ . This upturn is due to capillary condensation of nitrogen in mesopores with a narrow pore size distribution. The adsorption and desorption isotherms show hysteresis typical for cylindrical shaped mesopores. Barrett-Joyner-Halenda (BJH) analysis yielded an average mesopore diameter for Zeotile-4 of  $8.3 \pm 0.3$  nm (Figure 1, right). Alpha-s analysis revealed that the mesopore volume of Zeotile-4 was 1.33 mL/g. Zeotile-4 material thus exhibit two levels of porosity: microporosity and mesoporosity.




**Figure 1.** (left) Nitrogen physisorption isotherms of Zeotile-4 and Silicalite-1 crystals. The pressure ranges in which micropores and mesopores are filled are indicated. (right) Mesopore diameter distribution of Zeotile-4 calculated from the desorption isotherm using the BJH model.

Although Zeotile-4 crystals and Silicalite-1 zeolite crystals are both prepared starting from nanoslab sol, Silicalite-1 only exhibited microporosity due to the nanoslabs being densely packed, whereas the Zeotile-4 exhibited both microporosity and mesoporosity.

4. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: 8/7/2009

  
Alexander Aerts